April 24, 1974

J. H. Kreisher, Ph.D.
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The Council for Tobacco Research - USA, Inc.
110 East 59th Street
New York, N.Y. 10022

Dear John,

I am writing following up on Henderson's telephone call of last week.

Kouri is now relatively happy with his test and has instructed our immunologist (Dr. John Brown) how to do the test procedure up to the stage before adding BP, i.e., we separate the lymphocytes, add PHA and PW, then MC (or not) and finally freeze the samples for shipment to Kouri. The first batch of test sera goes off next week. These test sera are checking our technique, and variables such as numbers of cells in culture, amount of nitrogen required, glass v plastic, method of separation of cells. The results of these sera and others to be tested in the next 4-6 weeks should enable us to settle on a production method.

We trust therefore that we will start our field studies in early June.

We have received the go ahead to study AHH inducibility in patients from the six hospitals in Los Angeles County whose cooperation we had requested. The number of new patients diagnosed in 1972 with cancers of interest re AHH is given in Attachment #1. Initially we will concentrate on cancer of the lung (for obvious reaons), breast and pharynx (we have ongoing studies of these two sites), and then move on to studying the other sites. Detailed plans are given in Attachments #2 and #3.

Financial help from your Council would be of great assistance to us in completing these studies. We would therefore like to request from them funds for one year (in the first instance) as per

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Attachment #5. With these funds we will be able to process about 20 samples per week; projected completion dates of studies given on Attachments #2 and #3 are based on this requested level of funding.

Henderson mentioned that you may be able to consider funding this work on a monthly basis pending your Council's next relevant meeting. I would be grateful for your advice on how to proceed with this funding request.

Yours sincerely,

Malcolm C. Pike, Ph.D.
Professor, Community ;Medicine
and Pediatrics

P.S. The chemist here (Dr. Robert Gordon) and I have been doing some thinking about the possible (probable?) mechanism of AHH inducibility and cancer induction (see Attachment #4) and have come to the conclusion that measuring many more metabolites of BP might be very informative (method given in Science, 12 April 1974, 169-171). What are the possibilities of funding us to do this? Incidentally, if Kouri gets overwhelmed at MBA, Gordon sees no problem in completing Kouri's test here in L.A.

mcp/ml
Encl.

Attachment #1

#1972 Male Cases from CSP File by Site

Site	Hospital						
	USC/LAC	VA Wadsworth	VA Sepulveda	VA Long Beach	Kaiser Sunset	Harbor General	Total
Lung	127	55	57	82	57	46	424
Colon	15	15	17	19	48	11	125
Bladder	17	16	24	29	37	9	132
Esophagus	17	11	4	7	3	6	48
Mouth	24	7	2	15	12	1	61
Pharynx	15	11	2	16	7	3	54
Lip	4	11	1	6	3	0	25
Larynx	19	21	2	16	8	9	75

#1972 Female Cases from CSP File by Site

Site	Hospital			
	USC/LAC	Kaiser Sunset	Harbor General	Total
Lung	38	31	14	83
Breast	107	134	45	286
Colon	39	29	7	75
Bladder	13	8	1	22
Esophagus	9	4	3	16
Mouth	10	7	3	20
Pharynx	3	1	5	9
Larynx	5	4	2	11

Attachment #2

Lung Cancer

1. Hospital Study

We will interview 100 lung cancer patients (and take 15 ml blood sample) using a detailed questionnaire (Attachment #2.1, based on the Comprehensive Tobacco Questionnaire of the American Health Foundation and also including details of current medication). The patients will be interviewed soon after admission (when diagnosis may possibly still be in doubt). Clinical and pathological details on the patients will be obtained from hospital records.

100 matched hospital "controls" will also be interviewed in the same manner as the lung cancer patients. They will be sex, race, age matched within same 5-year age group, and will be drawn from the same hospital population. The controls will be chosen as the next new suitable patient entering the hospital with a non-neoplastic, non-respiratory disease.

We will analyze the results of the study in terms of smoking habits, tumor cell type, age and AHH inducibility (and base levels).

Adenocarcinoma of the lung is not thought to be related to cigarette smoking, but the relation of this cell type to AHH inducibility is of definite interest. Out of 100 lung cancer cases we expect only a few (10-20) adenocarcinomas, we will increase this number to 50 by selectively interviewing this type of case.

This study is projected to be completed by December, 1974.

2. Leisure World Study

We will test 100 long-term cigarette smokers over age 75 without cancer from the residents of "Leisure World", a retirement community south of Los Angeles County.

This study is projected to be completed by December, 1974.

The need for "controls" for this study will depend on whether we find an age and social class effect in our "controls" from the Hospital Study.

3. Environmental and Occupational Study

Depending on the answers to our questions on the measurement of AHH "base levels" (see attachment #4) we will look at these levels in high risk to lung cancer groups. In particular, we will look at the levels in persons exposed occupationally or at home to high levels of airborne PAH, and to persons in high risk to lung cancer trades (e.g. printers, painters, asbestos workers). This could give us a model for interaction between say smoking and asbestos exposure.

This study obviously cannot as yet be projected as regards time to completion.

Attachment #2 (cont'd.)

4. Ethnic Group Distribution Study

If the hospital study confirms the Kellerman, et al findings, then we will test in the first instance 100 healthy, young Mexican-Americans and 100 healthy young Anglo-whites to see if there is a difference in AHH levels in the two groups. Such a difference may be partly responsible for the lower rates of lung cancer in the Mexican-Americans in Los Angeles County.

This study is projected to be completed by May, 1975.

Attachment #3

Cancer at Other Sites

It is of obvious interest to check on the relationship between AHH and tumors of sites other than lung. In particular those sites that have been connected with smoking or with PAH induction in animals.

We will, therefore, interview and collect blood samples from 50 cases with cancer at each of the following sites: breast, pharynx, bladder, esophagus, larynx, colon, mouth, lip.

The breast cancer patients will be prevalent cases we have already interviewed for another study. They will be able to be collected by September, 1974.

The pharynx cancer patients will consist of both prevalent cases (about 25) we have already interviewed for another study and new cases reported to the hospitals given in Attachment #1.

Patients with tumors at one of the other sites will be obtained from these same six hospitals.

All these studies should be completed by May 1975.

Attachment #4

Basic Understanding of AHH Behavior

Further basic understanding of the mechanism of the correlation between AHH inducibility and lung cancer would help greatly to shape our approach to epidemiological studies. We feel particularly ignorant in this area.

The first question we would like an answer to is whether a person's base level of AHH activity in lymphocytes, i.e. no MC added to test, is affected by smoking or breathing PAH laden air? I.e., if I don't smoke for a week and the AHH activity in my lymphocytes is measured is it lower than it would be if I had smoked two packs a day for the week? If the answer is 'no', is it 'yes' for lung tissue AHH activity? The answer to the latter must (?) be 'yes'.

This first question is easy to answer and will do so in the next few months (unless we find that the answer is already known).

If we need to look at lung tissue AHH activity, could you please suggest to us how to do this.

The second question we have is why, if all BP is broken down through the same metabolic pathways independent (?) of AHH inducibility level is high AHH inducibility associated with cancer induction? I.e., if a person with high AHH inducibility simply converts the BP quicker but in no greater absolute amounts, why is he at higher risk? We are trying to get an understanding of this through discussions with local enzymologists but would welcome advice and/or information.

The third question is what drugs affect AHH levels? Antitumor agents? Barbiturates? What else? How do they affect levels? Can we use patients on these drugs in studies? It is obvious that we can answer some of these questions (as for question #1) but again we welcome advice and/or information.

Attachment #5

First Year Budget

	Cost	Sub-Total
Equipment		
Double viewing tube for Zeiss RA microscope	$± 500.	
Coulter counter (Model ZB1)	5,874.	$ 6,374.
Supplies		
Biologicals	$ 2,000.	
Chemicals	1,500.	
Glassware and disposables	3,000.	
Computing	1,000.	
Equipment maintenance	700.	
Phones	600.	
Incidentals (office supplies, xerox, postage, printing charges, reprints, etc.)	500.	
Airfreight	1,000.	$ 10,300.
Salaries		
Technician (Tech III)	11,000.	
Nurse/interviewer	13,700.	
Secretary/clerk (½ time)	4,000.	$ 28,700.
Travel		
Local (to hospitals, etc.)	2,000.	
Meetings, etc.	1,500.	$ 3,500.
Fringe benefits (12% of salaries and wages)		$ 3,444.
University overhead (15% of salaries and wages)		$ 6,375.
Total		$ 58,693.

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